

THE REMARKS

Claims 1, 4-9, 13-19, 21 and 22 were pending prior to entering the amendments.

The Amendments

Claim 1 is amended to recite a naturally occurring proteorhodopsin or a homolog thereof having at least 90% identity. Support for the amendment can be found, for example at page 9, line 30 through page 10, line 8.

New Claims 23 and 26 are supported by page 9, line 30 through page 10, line 8.

New Claims 25 and 27 supported by original Claims 1 and 4.

No new matter is added in the amendments. The Examiner is requested to enter the amendments.

Restriction Requirement

The key of this invention is that Applicant has discovered that a mutation in the conserved histidine of a naturally occurring proteorhodopsin provides a proteorhodopsin mutant with improved optical characteristics, i.e. has lower pK_{th} in comparison with the naturally occurring proteorhodopsin. Such technical feature was not taught or disclosed in any prior art.

The cited Reference US2007/0192889 (La Rosa et al) discloses a plant protein that only shows 7.6% sequence identity with the entire sequence of SEQ ID NO: 3, and 22.4% sequence similarity in a short stretch. A person with any bioinformatics training would not consider the plant protein being similar to a naturally occurring proteorhodopsin.

Furthermore, Applicant has amended Claim 1 to recite a naturally occurring proteorhodopsin or a homolog thereof having at least 90% identity. Clearly, the special technical feature of this invention has not been taught or suggested by La Rosa et al.

Because La Rosa et al. do not break the unity of invention, Applicants respectfully request that the Examiner reconsider the restriction requirement.

Claim Objection

Claims 4, 5 and 14 are objected for reciting non-electing subject matter.

As discussed above, Applicants believe that the amended Claim 1 is a proper linking claim. Thus, the non-electing subject matter should be rejoined.

35 U.S.C. 112, Second Paragraph Rejection

Claims 1, 4-5, 7-9, 14 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner states that the phrase "conserved histidine residue" in claim 1 (and its dependent claims 4-5, 7-8, 14) is unclear. The rejection is traversed because the phrase is explained throughout the application as follows.

A conserved histidine residue is at, for example, amino acid position 75 of Bac31A8, or position 77 of Hot75m1, or its equivalent position of a proteorhodopsin variant. (page 3, lines 19-20) FIGURES 3-1 to 3-8 depict an alignment of the amino acid sequences of 81 natural proteorhodopsin variants. The bold "H" indicates the position of a conserved histidine, which corresponds to H75 of Bac31A8. (Page 9, lines 5-7) Conserved amino acid residues that are involved in the relay of protons through the all-trans-retinal binding site, but are not in direct contact with the all-trans-retinal cofactor, are likely to affect the pH dependent spectral shift and the pK_{rh} value of proteorhodopsin, and allow for a continued pumping of protons and therefore a productive photocycle. Applicants have identified such conserved amino acid residues in proteorhodopsins. (Page 18, lines 7-11)

A conserved amino acid residue of proteorhodopsin is an amino acid that is found in the equivalent position of the 81 proteorhodopsins as depicted in FIGURE 3. FIGURE 3 shows the alignment of amino acid sequences of 81 natural proteorhodopsin variants. Examples of conserved amino acid residues (H75) are shown in FIGURE 3. Such conserved amino acid residues can affect the conformation of the protein and the positioning of the all-trans-retinal molecule in relation to the proteorhodopsin protein. (page 18, lines 24-31)

As shown in Figure 3, naturally occurring proteorhodopsins have high degree of homology. Applicants have shown "the conserved histidine" in 81 naturally occurring proteorhodopsins. **A skilled person in the art can easily compare and align the amino acid sequence of any naturally occurring proteorhodopsin with the 81 amino acid sequences in**

Figure 3 and determine what the conserved histidine is.

Therefore, the phrase “the conserved histidine” in a naturally occurring proteorhodopsin is not indefinite.

The Examiner states that the phrase "wild type proteorhodopsin variants" in claim 1 (and its dependent claims 4-5, 7-8, 14) is vague. Applicants have used wild type proteorhodopsins and naturally occurring proteorhodopsins interchangeably in the application. To be consistent, Applicants have amended the claims to recite a naturally occurring proteorhodopsin.

Claims 4 is rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants have amended Claim 1 to recite a naturally occurring proteorhodopsin or a homolog thereof having at least 90% identity.

Therefore, the §112, second paragraph rejection of Claims 1, 4-5, 7-9, 14 should be withdrawn.

35 U.S.C. 112, First Paragraph Rejection

Claims 1, 5, 7-9 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner states that Claim 1 is directed to genus of mutants which have been inadequately described in the specification. The Examiner also states that Applicant is claiming a genus of products by what they do rather than what they are, which fails to meet the written description requirements. The rejection is traversed in parts and overcome in parts in view of the claim amendment.

Naturally occurring proteorhodopsins have known and defined amino acid sequences. Naturally occurring proteorhodopsins have similar amino acid sequences as illustrated by the 81 sequences in Figure 3. Figure 3 also shows the amino acid sequence alignment of 81 naturally occurring proteorhodopsins and the conserved histidine residue. It is not possible for Applicant to list the amino acid sequences of all naturally occurring

proteorhodopsins and show the alignments of the sequences to demonstrate the conserved histidine. However, **Applicant has provided a large representative number of species.**

Applicant is claiming a genus of products by what they are, i.e., a proteorhodopsin mutant having a mutation in the conserved histidine residue of a naturally occurring proteorhodopsin. A person skilled in the art can easily pick a naturally occurring proteorhodopsin, compare its sequence with those in Figure 3 and determine what the claimed product is. A person skilled in the art would agree that Applicant had possession of the claimed product when the application was filed.

Therefore, the written description requirement of Claims 1, 5, 7-9 is fulfilled.

35 U.S.C. 102(e) Rejection

Claim 1 is rejected under 35 U.S.C. §102(e) as allegedly being anticipated by La Rosa et al. (U.S. Publication No. US2007/0192889). The rejection is traversed.

Claim 1 is directed to a proteorhodopsin mutant comprising a mutation in a conserved histidine residue of a naturally occurring proteorhodopsin or a homolog thereof having at least 90% identity,

The cited Reference US2007/0192889 (La Rosa et al) discloses a plant protein that only shows 7.6% sequence identity with the entire sequence of SEQ ID NO: 3, and 22.4% sequence similarity in a short stretch. When the sequence of the La Rosa protein is aligned and compared with the 81 naturally occurring proteorhodopsins in Figure 3, it is clear that the La Rosa protein is **not** a proteorhodopsin mutant comprising a mutation in a conserved histidine residue of a naturally occurring proteorhodopsin or a homolog thereof having at least 90% identity.


Therefore, the 102(e) rejection of Claim 1 over La Rosa et al should be withdrawn.

CONCLUSION

Applicants believe that the application is now in good and proper condition for allowance. Early notification of allowance is earnestly solicited.

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Respectfully submitted,



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